

P023P01.ST25.txt
SEQUENCE LISTING

<110> Japan Science and Technology Corporation
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Tanizawa, Katsuyuki
Kondo, Akihiko
Ueda, Masakazu
Seno, Masaharu
Tada, Hiroko

<120> DRUG CONTAINING HOLLOW PROTEIN NANOPARTICLES OF PARTICLE-FORMING
PROTEIN, FUSED WITH DISEASE-TREATING TARGET-CELL-SUBSTANCE

<130> P023P01/US

<140> US 10/509,247
<141> 2004-09-28

<150> PCT/JP03/02602
<151> 2003-03-05

<150> JP2002-97280
<151> 2002-03-29

<160> 20

<170> PatentIn version 3.3

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Thr Val Trp Leu Ser Val Ile Trp Met Met Trp Tyr Trp Gly Pro Ser
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Arg Ala Glu Val Lys Phe Glu Gly Asp Thr Leu Val Asn Arg Ile Glu
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595 600 605

Gly Asp Gly Pro Val Leu Leu Pro Asp Asn His Tyr Leu Ser Thr Gln
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agg Arg	agg Arg 540	tac Tyr	ttc Phe	cag Gln	gga Gly	atc Ile 545	cgt Arg	gtc Val	tac Tyr	ctg Leu	aaa Lys 550	gag Glu	aag Lys	aaa Lys	tac Tyr	1684
agc Ser 555	gac Asp	tgt Cys	gcc Ala	tgg Trp	gaa Glu 560	gtt Val	gtc Val	aga Arg	atg Met	gaa Glu 565	atc Ile	atg Met	aaa Lys	tcc Ser	ttg Leu 570	1732

P023P01.ST25.txt

ttc tta tca aca aac atg caa gaa aga ctg aga agt aaa gat aga gac 1780
Phe Leu Ser Thr Asn Met Gln Glu Arg Leu Arg Ser Lys Asp Arg Asp
575 580 585

ctg ggc tca tct tga gcggccgc 1803
Leu Gly Ser Ser
590

<210> 16
<211> 590
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic Construct
<400> 16

Met Arg Ser Leu Leu Ile Leu Val Leu Cys Phe Leu Pro Leu Ala Ala
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Leu Gly Lys Val Arg Gln Gly Met Gly Thr Asn Leu Ser Val Pro Asn
20 25 30

Pro Leu Gly Phe Phe Pro Asp His Gln Leu Asp Pro Ala Phe Gly Ala
35 40 45

Asn Ser Asn Asn Pro Asp Trp Asp Phe Asn Pro Asn Lys Asp Gln Trp
50 55 60

Pro Glu Ala Asn Gln Val Gly Ala Gly Ala Phe Gly Pro Gly Phe Thr
65 70 75 80

Pro Pro His Gly Gly Leu Leu Gly Trp Ser Pro Gln Ala Gln Gly Ile
85 90 95

Leu Thr Thr Val Pro Ala Ala Pro Pro Pro Ala Ser Thr Asn Arg Gln
100 105 110

Ser Gly Arg Gln Pro Thr Pro Ile Ser Pro Pro Leu Arg Asp Ser His
115 120 125

Pro Gln Ala Met Gln Trp Asn Ser Thr Thr Phe His Gln Ala Leu Leu
130 135 140

Asp Pro Arg Val Arg Gly Leu Tyr Phe Pro Ala Gly Gly Ser Ser Ser
145 150 155 160

Gly Thr Val Asn Pro Val Pro Thr Thr Ala Ser Pro Ile Ser Gly Asp
165 170 175

P023P01.ST25.txt

Pro Ala Pro Asn Met Glu Asn Thr Thr Ser Gly Phe Leu Gly Pro Leu
180 185 190

Leu Val Leu Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile
195 200 205

Pro Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly
210 215 220

Ala Pro Thr Cys Pro Gly Gln Asn Ser Gln Ser Pro Thr Ser Asn His
225 230 235 240

Ser Pro Thr Ser Cys Pro Pro Ile Cys Pro Gly Tyr Arg Trp Met Cys
245 250 255

Leu Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile
260 265 270

Phe Leu Leu Val Leu Leu Asp Tyr Gln Gly Met Leu Pro Val Cys Pro
275 280 285

Leu Leu Pro Gly Thr Ser Thr Thr Ser Thr Gly Pro Cys Lys Thr Cys
290 295 300

Thr Ile Pro Ala Gln Gly Thr Ser Met Phe Pro Ser Cys Cys Cys Thr
305 310 315 320

Lys Pro Ser Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp
325 330 335

Ala Phe Ala Arg Phe Leu Trp Glu Trp Ala Ser Val Arg Phe Ser Trp
340 345 350

Leu Ser Leu Leu Val Pro Phe Val Gln Trp Phe Val Gly Leu Ser Pro
355 360 365

Thr Val Trp Leu Ser Val Ile Trp Met Met Trp Tyr Trp Gly Pro Ser
370 375 380

Leu Tyr Asn Ile Leu Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe
385 390 395 400

Cys Leu Trp Val Tyr Ile Asp Tyr Lys Asp Asp Asp Asp Lys Ile Pro
405 410 415

Val Gly Cys Asp Leu Pro Gln Asn His Gly Leu Leu Ser Arg Asn Thr
420 425 430

P023P01.ST25.txt

Leu Val Leu Leu His Gln Met Arg Arg Ile Ser Pro Phe Leu Cys Leu
435 440 445

Lys Asp Arg Arg Asp Phe Arg Phe Pro Gln Glu Met Val Lys Gly Ser
450 455 460

Gln Leu Gln Lys Ala His Val Met Ser Val Leu His Glu Met Leu Gln
465 470 475 480

Gln Ile Phe Ser Leu Phe His Thr Glu Arg Ser Ser Ala Ala Trp Asn
485 490 495

Met Thr Leu Leu Asp Gln Leu His Thr Gly Leu His Gln Gln Leu Gln
500 505 510

His Leu Glu Thr Cys Leu Leu Gln Val Val Gly Glu Gly Glu Ser Ala
515 520 525

Gly Ala Ile Ser Ser Pro Ala Leu Thr Leu Arg Arg Tyr Phe Gln Gly
530 535 540

Ile Arg Val Tyr Leu Lys Glu Lys Lys Tyr Ser Asp Cys Ala Trp Glu
545 550 555 560

Val Val Arg Met Glu Ile Met Lys Ser Leu Phe Leu Ser Thr Asn Met
565 570 575

Gln Glu Arg Leu Arg Ser Lys Asp Arg Asp Leu Gly Ser Ser
580 585 590

<210> 17
<211> 1779
<212> DNA
<213> Artificial Sequence

<220>
<223> IFNfA gene fused with HBsAg L protein

<220>
<221> CDS
<222> (23)..(1771)
<223> IFNfA gene fused with HBsAg L protein gene

<400> 17
ctcgaggtcg agtataaaaa ca atg aga tct ttg ttg atc ttg gtt ttg tgt 52
Met Arg Ser Leu Leu Ile Leu Val Leu Cys
1 5 10

ttc ttg cca ttg gct gct ttg ggt aag gtt cga caa ggc atg ggg acg 100
Phe Leu Pro Leu Ala Ala Leu Gly Lys Val Arg Gln Gly Met Gly Thr
15 20 25

P023P01.ST25.txt

aat ctt tct gtt ccc aat cct ctg gga ttc ttt ccc gat cac cag ttg Asn Leu Ser Val Pro Asn Pro Leu Gly Phe Phe Pro Asp His Gln Leu 30 35 40	148
gac cct gcg ttc gga gcc aac tca aac aat cca gat tgg gac ttc aac Asp Pro Ala Phe Gly Ala Asn Ser Asn Asn Pro Asp Trp Asp Phe Asn 45 50 55	196
ccc aac aag gat caa tgg cca gag gca aat cag gta gga gcg gga gca Pro Asn Lys Asp Gln Trp Pro Glu Ala Asn Gln Val Gly Ala Gly Ala 60 65 70	244
ttc ggg cca ggg ttc acc cca cca cac ggc ggt ctt ttg ggg tgg agc Phe Gly Pro Gly Phe Thr Pro Pro His Gly Gly Leu Leu Gly Trp Ser 75 80 85 90	292
cct cag gct cag ggc ata ttg aca aca gtg cca gca gca cct cct cct Pro Gln Ala Gln Gly Ile Leu Thr Thr Val Pro Ala Ala Pro Pro Pro 95 100 105	340
gcc tcc acc aat cgg cag tca gga aga cag cct act ccc atc tct cca Ala Ser Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro Ile Ser Pro 110 115 120	388
cct cta aga gac agt cat cct cag gcc atg cag tgg aat tcc aca aca Pro Leu Arg Asp Ser His Pro Gln Ala Met Gln Trp Asn Ser Thr Thr 125 130 135	436
ttc cac caa gct ctg cta gat ccc aga gtg agg ggc cta tat ttt cct Phe His Gln Ala Leu Leu Asp Pro Arg Val Arg Gly Leu Tyr Phe Pro 140 145 150	484
gct ggt ggc tcc agt tcc gga aca gta aac cct gtt ccg act act gcc Ala Gly Gly Ser Ser Ser Gly Thr Val Asn Pro Val Pro Thr Thr Ala 155 160 165 170	532
tca ccc ata tct ggg gac cct gca ccg aac atg gag aac aca aca tca Ser Pro Ile Ser Gly Asp Pro Ala Pro Asn Met Glu Asn Thr Thr Ser 175 180 185	580
gga ttc cta gga ccc ctg ctc gtg tta cag gcg ggg ttt ttc ttg ttg Gly Phe Leu Gly Pro Leu Leu Val Leu Gln Ala Gly Phe Phe Leu Leu 190 195 200	628
aca aga atc ctc aca ata cca cag agt cta gac tcg tgg tgg act tct Thr Arg Ile Leu Thr Ile Pro Gln Ser Leu Asp Ser Trp Trp Thr Ser 205 210 215	676
ctc aat ttt cta ggg gga gca ccc acg tgt cct ggc caa aat tcg cag Leu Asn Phe Leu Gly Gly Ala Pro Thr Cys Pro Gly Gln Asn Ser Gln 220 225 230	724
tcc cca acc tcc aat cac tca cca acc tct tgt cct cca att tgt cct Ser Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro Pro Ile Cys Pro 235 240 245 250	772
ggc tat cgc tgg atg tgt ctg cgg cgt ttt atc ata ttc ctc ttc atc Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe Ile Ile Phe Leu Phe Ile 255 260 265	820
ctg ctg cta tgc ctc atc ttc ttg ttg gtt ctt ctg gac tac caa ggt Leu Leu Leu Cys Leu Ile Phe Leu Leu Val Leu Leu Asp Tyr Gln Gly 265 270 275 280	868

P023P01.ST25.txt

270										275					280					
atg	ttg	ccc	ggt	tgt	cct	cta	ctt	cca	gga	aca	tca	acc	acc	agc	acg	916				
Met	Leu	Pro	Val	Cys	Pro	Leu	Leu	Pro	Gly	Thr	Ser	Thr	Thr	Ser	Thr					
		285					290					295								
ggg	cca	tgc	aag	acc	tgc	acg	att	cct	gct	caa	gga	acc	tct	atg	ttt	964				
Gly	Pro	Cys	Lys	Thr	Cys	Thr	Ile	Pro	Ala	Gln	Gly	Thr	Ser	Met	Phe					
	300					305					310									
ccc	tct	tgt	tgc	tgt	aca	aaa	cct	tcg	gac	gga	aac	tgc	act	tgt	att	1012				
Pro	Ser	Cys	Cys	Cys	Thr	Lys	Pro	Ser	Asp	Gly	Asn	Cys	Thr	Cys	Ile					
315					320					325					330					
ccc	atc	cca	tca	tcc	tgg	gct	ttc	gca	aga	ttc	cta	tgg	gag	tgg	gcc	1060				
Pro	Ile	Pro	Ser	Ser	Trp	Ala	Phe	Ala	Arg	Phe	Leu	Trp	Glu	Trp	Ala					
				335					340					345						
tca	gtc	cgt	ttc	tcc	tgg	ctc	agt	tta	cta	gtg	cca	ttt	gtt	cag	tgg	1108				
Ser	Val	Arg	Phe	Ser	Trp	Leu	Ser	Leu	Leu	Val	Pro	Phe	Val	Gln	Trp					
			350					355					360							
ttc	gta	ggg	ctt	tcc	ccc	act	gtt	tgg	ctt	tca	gtt	ata	tgg	atg	atg	1156				
Phe	Val	Gly	Leu	Ser	Pro	Thr	Val	Trp	Leu	Ser	Val	Ile	Trp	Met	Met					
		365					370					375								
tgg	tat	tgg	ggg	cca	agt	ctg	tac	aac	atc	ttg	agt	ccc	ttt	tta	cct	1204				
Trp	Tyr	Trp	Gly	Pro	Ser	Leu	Tyr	Asn	Ile	Leu	Ser	Pro	Phe	Leu	Pro					
	380					385					390									
cta	tta	cca	att	ttc	ttt	tgt	ctt	tgg	gta	tat	att	gat	tac	aag	gat	1252				
Leu	Leu	Pro	Ile	Phe	Phe	Cys	Leu	Trp	Val	Tyr	Ile	Asp	Tyr	Lys	Asp					
395					400					405					410					
gac	gac	gat	aag	ata	ccg	gtg	agc	tac	aac	ttg	ctt	gga	ttc	cta	caa	1300				
Asp	Asp	Asp	Lys	Ile	Pro	Val	Ser	Tyr	Asn	Leu	Leu	Gly	Phe	Leu	Gln					
				415					420					425						
aga	agc	agc	aat	ttt	cag	tgt	cag	aag	ctc	ctg	tgg	caa	ttg	aat	ggg	1348				
Arg	Ser	Ser	Asn	Phe	Gln	Cys	Gln	Lys	Leu	Leu	Trp	Gln	Leu	Asn	Gly					
			430					435					440							
agg	ctt	gaa	tac	tgc	ctc	aag	gac	agg	atg	aac	ttt	gac	atc	cct	gag	1396				
Arg	Leu	Glu	Tyr	Cys	Leu	Lys	Asp	Arg	Met	Asn	Phe	Asp	Ile	Pro	Glu					
		445					450					455								
gag	att	aag	cag	ctg	cag	cag	ttc	cag	aag	gag	gac	gcc	gca	ttg	acc	1444				
Glu	Ile	Lys	Gln	Leu	Gln	Gln	Phe	Gln	Lys	Glu	Asp	Ala	Ala	Leu	Thr					
	460					465					470									
atc	tat	gag	atg	ctc	cag	aac	atc	ttt	gct	att	ttc	aga	caa	gat	tca	1492				
Ile	Tyr	Glu	Met	Leu	Gln	Asn	Ile	Phe	Ala	Ile	Phe	Arg	Gln	Asp	Ser					
475					480					485					490					
tct	agc	act	ggc	tgg	aat	gag	act	att	gtt	gag	aac	ctc	ctg	gct	aat	1540				
Ser	Ser	Thr	Gly	Trp	Asn	Glu	Thr	Ile	Val	Glu	Asn	Leu	Leu	Ala	Asn					
				495					500					505						
gtc	tat	cat	cag	ata	aac	cat	ctg	aag	aca	gtc	ctg	gaa	gaa	aaa	ctg	1588				
Val	Tyr	His	Gln	Ile	Asn	His	Leu	Lys	Thr	Val	Leu	Glu	Glu	Lys	Leu					
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gag	aaa	gaa	gat	ttc	acc	agg	gga	aaa	ctc	atg	agc	agt	ctg	cac	ctg	1636				

P023P01.ST25.txt

Glu	Lys	Glu	Asp	Phe	Thr	Arg	Gly	Lys	Leu	Met	Ser	Ser	Leu	His	Leu		
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aaa	aga	tat	tat	ggg	agg	att	ctg	cat	tac	ctg	aag	gcc	aag	gag	tac	1684	
Lys	Arg	Tyr	Tyr	Gly	Arg	Ile	Leu	His	Tyr	Leu	Lys	Ala	Lys	Glu	Tyr		
		540				545					550						
agt	cac	tgt	gcc	tgg	acc	ata	gtc	aga	gtg	gaa	atc	cta	agg	aac	ttt	1732	
Ser	His	Cys	Ala	Trp	Thr	Ile	Val	Arg	Val	Glu	Ile	Leu	Arg	Asn	Phe		
		555			560					565					570		
tac	ttc	att	aac	aga	ctt	aca	ggg	tac	ctc	cga	aac	tga	gcggccgc			1779	
Tyr	Phe	Ile	Asn	Arg	Leu	Thr	Gly	Tyr	Leu	Arg	Asn						
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<210> 18
 <211> 582
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic Construct

<400> 18

Met	Arg	Ser	Leu	Leu	Ile	Leu	Val	Leu	Cys	Phe	Leu	Pro	Leu	Ala	Ala
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Leu	Gly	Lys	Val	Arg	Gln	Gly	Met	Gly	Thr	Asn	Leu	Ser	Val	Pro	Asn
		20						25					30		

Pro	Leu	Gly	Phe	Phe	Pro	Asp	His	Gln	Leu	Asp	Pro	Ala	Phe	Gly	Ala
		35					40					45			

Asn	Ser	Asn	Asn	Pro	Asp	Trp	Asp	Phe	Asn	Pro	Asn	Lys	Asp	Gln	Trp
	50					55					60				

Pro	Glu	Ala	Asn	Gln	Val	Gly	Ala	Gly	Ala	Phe	Gly	Pro	Gly	Phe	Thr
65					70				75						80

Pro	Pro	His	Gly	Gly	Leu	Leu	Gly	Trp	Ser	Pro	Gln	Ala	Gln	Gly	Ile
			85						90					95	

Leu	Thr	Thr	Val	Pro	Ala	Ala	Pro	Pro	Pro	Ala	Ser	Thr	Asn	Arg	Gln
			100					105					110		

Ser	Gly	Arg	Gln	Pro	Thr	Pro	Ile	Ser	Pro	Pro	Leu	Arg	Asp	Ser	His
		115					120					125			

Pro	Gln	Ala	Met	Gln	Trp	Asn	Ser	Thr	Thr	Phe	His	Gln	Ala	Leu	Leu
		130				135					140				

Asp	Pro	Arg	Val	Arg	Gly	Leu	Tyr	Phe	Pro	Ala	Gly	Gly	Ser	Ser	Ser

145 150 155 160
 Gly Thr Val Asn Pro Val Pro Thr Thr Ala Ser Pro Ile Ser Gly Asp
 165 170 175
 Pro Ala Pro Asn Met Glu Asn Thr Thr Ser Gly Phe Leu Gly Pro Leu
 180 185 190
 Leu Val Leu Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile
 195 200 205
 Pro Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly
 210 215 220
 Ala Pro Thr Cys Pro Gly Gln Asn Ser Gln Ser Pro Thr Ser Asn His
 225 230 235 240
 Ser Pro Thr Ser Cys Pro Pro Ile Cys Pro Gly Tyr Arg Trp Met Cys
 245 250 255
 Leu Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile
 260 265 270
 Phe Leu Leu Val Leu Leu Asp Tyr Gln Gly Met Leu Pro Val Cys Pro
 275 280 285
 Leu Leu Pro Gly Thr Ser Thr Thr Ser Thr Gly Pro Cys Lys Thr Cys
 290 295 300
 Thr Ile Pro Ala Gln Gly Thr Ser Met Phe Pro Ser Cys Cys Cys Thr
 305 310 315 320
 Lys Pro Ser Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp
 325 330 335
 Ala Phe Ala Arg Phe Leu Trp Glu Trp Ala Ser Val Arg Phe Ser Trp
 340 345 350
 Leu Ser Leu Leu Val Pro Phe Val Gln Trp Phe Val Gly Leu Ser Pro
 355 360 365
 Thr Val Trp Leu Ser Val Ile Trp Met Met Trp Tyr Trp Gly Pro Ser
 370 375 380
 Leu Tyr Asn Ile Leu Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe
 385 390 395 400

Cys Leu Trp Val Tyr Ile Asp Tyr Lys Asp Asp Asp Asp Lys Ile Pro
405 410 415

Val Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
420 425 430

Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu
435 440 445

Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
450 455 460

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
465 470 475 480

Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
485 490 495

Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
500 505 510

His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr
515 520 525

Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg
530 535 540

Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr
545 550 555 560

Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu
565 570 575

Thr Gly Tyr Leu Arg Asn
580

<210> 19
<211> 3359
<212> DNA
<213> Artificial Sequence

<220>
<223> HGF gene fused with HBsAg L protein

<220>
<221> CDS
<222> (23)..(3352)
<223> HGF gene fused with HBsAg L protein gene

<400> 19

P023P01.ST25.txt

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Met Arg Ser Leu Leu Ile Leu Val Leu Cys	
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Phe Leu Pro Leu Ala Ala Leu Gly Lys Val Arg Gln Gly Met Gly Thr	
15 20 25	
aat ctt tct gtt ccc aat cct ctg gga ttc ttt ccc gat cac cag ttg	148
Asn Leu Ser Val Pro Asn Pro Leu Gly Phe Phe Pro Asp His Gln Leu	
30 35 40	
gac cct gcg ttc gga gcc aac tca aac aat cca gat tgg gac ttc aac	196
Asp Pro Ala Phe Gly Ala Asn Ser Asn Asn Pro Asp Trp Asp Phe Asn	
45 50 55	
ccc aac aag gat caa tgg cca gag gca aat cag gta gga gcg gga gca	244
Pro Asn Lys Asp Gln Trp Pro Glu Ala Asn Gln Val Gly Ala Gly Ala	
60 65 70	
ttc ggg cca ggg ttc acc cca cca cac ggc ggt ctt ttg ggg tgg agc	292
Phe Gly Pro Gly Phe Thr Pro Pro His Gly Gly Leu Leu Gly Trp Ser	
75 80 85 90	
cct cag gct cag ggc ata ttg aca aca gtg cca gca gca cct cct cct	340
Pro Gln Ala Gln Gly Ile Leu Thr Thr Val Pro Ala Ala Pro Pro Pro	
95 100 105	
gcc tcc acc aat cgg cag tca gga aga cag cct act ccc atc tct cca	388
Ala Ser Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro Ile Ser Pro	
110 115 120	
cct cta aga gac agt cat cct cag gcc atg cag tgg aat tcc aca aca	436
Pro Leu Arg Asp Ser His Pro Gln Ala Met Gln Trp Asn Ser Thr Thr	
125 130 135	
ttc cac caa gct ctg cta gat ccc aga gtg agg ggc cta tat ttt cct	484
Phe His Gln Ala Leu Leu Asp Pro Arg Val Arg Gly Leu Tyr Phe Pro	
140 145 150	
gct ggt ggc tcc agt tcc gga aca gta aac cct gtt ccg act act gcc	532
Ala Gly Gly Ser Ser Ser Gly Thr Val Asn Pro Val Pro Thr Thr Ala	
155 160 165 170	
tca ccc ata tct ggg gac cct gca ccg aac atg gag aac aca aca tca	580
Ser Pro Ile Ser Gly Asp Pro Ala Pro Asn Met Glu Asn Thr Thr Ser	
175 180 185	
gga ttc cta gga ccc ctg ctc gtg tta cag gcg ggg ttt ttc ttg ttg	628
Gly Phe Leu Gly Pro Leu Leu Val Leu Gln Ala Gly Phe Phe Leu Leu	
190 195 200	
aca aga atc ctc aca ata cca cag agt cta gac tcg tgg tgg act tct	676
Thr Arg Ile Leu Thr Ile Pro Gln Ser Leu Asp Ser Trp Trp Thr Ser	
205 210 215	
ctc aat ttt cta ggg gga gca ccc acg tgt cct ggc caa aat tcg cag	724
Leu Asn Phe Leu Gly Gly Ala Pro Thr Cys Pro Gly Gln Asn Ser Gln	
220 225 230	
tcc cca acc tcc aat cac tca cca acc tct tgt cct cca att tgt cct	772
Ser Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro Pro Ile Cys Pro	
235 240 245 250	

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ggc	tat	cg	tgg	atg	tgt	ctg	cg	cg	ttt	atc	ata	ttc	ctc	ttc	atc	820
Gly	Tyr	Arg	Trp	Met	Cys	Leu	Arg	Arg	Phe	Ile	Ile	Phe	Leu	Phe	Ile	
				255					260					265		
ctg	ctg	cta	tgc	ctc	atc	ttc	ttg	ttg	gtt	ctt	ctg	gac	tac	caa	ggt	868
Leu	Leu	Leu	Cys	Leu	Ile	Phe	Leu	Leu	Val	Leu	Leu	Asp	Tyr	Gln	Gly	
			270					275					280			
atg	ttg	ccc	gtt	tgt	cct	cta	ctt	cca	gga	aca	tca	acc	acc	agc	acg	916
Met	Leu	Pro	Val	Cys	Pro	Leu	Leu	Pro	Gly	Thr	Ser	Thr	Thr	Ser	Thr	
		285					290					295				
ggg	cca	tgc	aag	acc	tgc	acg	att	cct	gct	caa	gga	acc	tct	atg	ttt	964
Gly	Pro	Cys	Lys	Thr	Cys	Thr	Ile	Pro	Ala	Gln	Gly	Thr	Ser	Met	Phe	
	300					305					310					
ccc	tct	tgt	tgc	tgt	aca	aaa	cct	tcg	gac	gga	aac	tgc	act	tgt	att	1012
Pro	Ser	Cys	Cys	Cys	Thr	Lys	Pro	Ser	Asp	Gly	Asn	Cys	Thr	Cys	Ile	
					320					325					330	
ccc	atc	cca	tca	tcc	tgg	gct	ttc	gca	aga	ttc	cta	tgg	gag	tgg	gcc	1060
Pro	Ile	Pro	Ser	Ser	Trp	Ala	Phe	Ala	Arg	Phe	Leu	Trp	Glu	Trp	Ala	
				335					340					345		
tca	gtc	cg	ttc	tcc	tgg	ctc	agt	tta	cta	gtg	cca	ttt	gtt	cag	tgg	1108
Ser	Val	Arg	Phe	Ser	Trp	Leu	Ser	Leu	Leu	Val	Pro	Phe	Val	Gln	Trp	
			350					355					360			
ttc	gta	ggg	ctt	tcc	ccc	act	gtt	tgg	ctt	tca	gtt	ata	tgg	atg	atg	1156
Phe	Val	Gly	Leu	Ser	Pro	Thr	Val	Trp	Leu	Ser	Val	Ile	Trp	Met	Met	
		365					370					375				
tgg	tat	tgg	ggg	cca	agt	ctg	tac	aac	atc	ttg	agt	ccc	ttt	tta	cct	1204
Trp	Tyr	Trp	Gly	Pro	Ser	Leu	Tyr	Asn	Ile	Leu	Ser	Pro	Phe	Leu	Pro	
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Glu	Phe	Lys	Lys	Ser	Ala	Lys	Thr	Thr	Leu	Ile	Lys	Ile	Asp	Pro	Ala	
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Leu	Lys	Ile	Lys	Thr	Lys	Lys	Val	Asn	Thr	Ala	Asp	Gln	Cys	Ala	Asn	
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Arg	Cys	Thr	Arg	Asn	Lys	Gly	Leu	Pro	Phe	Thr	Cys	Lys	Ala	Phe	Val	
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Phe	Asp	Lys	Ala	Arg	Lys	Gln	Cys	Leu	Trp	Phe	Pro	Phe	Asn	Ser	Met	
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Asn	Lys	Asp	Tyr	Ile	Arg	Asn	Cys	Ile	Ile	Gly	Lys	Gly	Arg	Ser	Tyr	
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Lys	Gly	Thr	Val	Ser	Ile	Thr	Lys	Ser	Gly	Ile	Lys	Cys	Gln	Pro	Trp	
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Ser	Ser	Met	Ile	Pro	His	Glu	His	Ser	Tyr	Arg	Gly	Lys	Asp	Leu	Gln	
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Phe	Thr	Ser	Asn	Pro	Glu	Val	Arg	Tyr	Glu	Val	Cys	Asp	Ile	Pro	Gln	
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Cys	Ser	Glu	Val	Glu	Cys	Met	Thr	Cys	Asn	Gly	Glu	Ser	Tyr	Arg	Gly	
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Gln	Thr	Pro	His	Arg	His	Lys	Phe	Leu	Pro	Glu	Arg	Tyr	Pro	Asp	Lys	
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Lys	Thr	Cys	Ala	Asp	Asn	Thr	Met	Asn	Asp	Thr	Asp	Val	Pro	Leu	Glu	
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Phe	Thr	Thr	Asp	Pro	Asn	Ile	Arg	Val	Gly	Tyr	Cys	Ser	Gln	Ile	Pro	
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Asp	Ala	His	Gly	Pro	Trp	Cys	Tyr	Thr	Gly	Asn	Pro	Leu	Ile	Pro	Trp	
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Asp	Tyr	Cys	Pro	Ile	Ser	Arg	Cys	Glu	Gly	Asp	Thr	Thr	Pro	Thr	Ile	
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Lys	Asp	Tyr	Glu	Ala	Trp	Leu	Gly	Ile	His	Asp	Val	His	Gly	Arg	Gly	
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Leu Asn Glu	Ser Glu Ile Cys Ala	Gly Ala Glu Lys Ile	Gly Ser	
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Gly Pro Cys	Glu Gly Asp Tyr Gly	Gly Pro Leu Val Cys	Glu Gln	
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His Lys Met	Arg Met Val Leu Gly	Val Ile Val Pro Gly	Arg Gly	
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Cys Ala Ile	Pro Asn Arg Pro Gly	Ile Phe Val Arg Val	Ala Tyr	
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tat gca aaa	tgg ata cac aaa att	att tta aca tat aag	gta cca	3343
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Gln Ser				

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Pro Leu Gly Phe Phe Pro Asp His Gln Leu Asp Pro Ala Phe Gly Ala
 35 40 45

Asn Ser Asn Asn Pro Asp Trp Asp Phe Asn Pro Asn Lys Asp Gln Trp
 50 55 60

Pro Glu Ala Asn Gln Val Gly Ala Gly Ala Phe Gly Pro Gly Phe Thr
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Pro Pro His Gly Gly Leu Leu Gly Trp Ser Pro Gln Ala Gln Gly Ile
85 90 95

Leu Thr Thr Val Pro Ala Ala Pro Pro Pro Ala Ser Thr Asn Arg Gln
100 105 110

Ser Gly Arg Gln Pro Thr Pro Ile Ser Pro Pro Leu Arg Asp Ser His
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Pro Gln Ala Met Gln Trp Asn Ser Thr Thr Phe His Gln Ala Leu Leu
130 135 140

Asp Pro Arg Val Arg Gly Leu Tyr Phe Pro Ala Gly Gly Ser Ser Ser
145 150 155 160

Gly Thr Val Asn Pro Val Pro Thr Thr Ala Ser Pro Ile Ser Gly Asp
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Pro Ala Pro Asn Met Glu Asn Thr Thr Ser Gly Phe Leu Gly Pro Leu
180 185 190

Leu Val Leu Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile
195 200 205

Pro Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly
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Ala Pro Thr Cys Pro Gly Gln Asn Ser Gln Ser Pro Thr Ser Asn His
225 230 235 240

Ser Pro Thr Ser Cys Pro Pro Ile Cys Pro Gly Tyr Arg Trp Met Cys
245 250 255

Leu Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile
260 265 270

Phe Leu Leu Val Leu Leu Asp Tyr Gln Gly Met Leu Pro Val Cys Pro
275 280 285

Leu Leu Pro Gly Thr Ser Thr Thr Ser Thr Gly Pro Cys Lys Thr Cys
290 295 300

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305 310 315 320

Lys Pro Ser Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp
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Ala Phe Ala Arg Phe Leu Trp Glu Trp Ala Ser Val Arg Phe Ser Trp
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Leu Ser Leu Leu Val Pro Phe Val Gln Trp Phe Val Gly Leu Ser Pro
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370 375 380

Leu Tyr Asn Ile Leu Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe
385 390 395 400

Cys Leu Trp Val Tyr Ile Asp Tyr Lys Asp Asp Asp Asp Lys Ile Pro
405 410 415

Val Gln Arg Lys Arg Arg Asn Thr Ile His Glu Phe Lys Lys Ser Ala
420 425 430

Lys Thr Thr Leu Ile Lys Ile Asp Pro Ala Leu Lys Ile Lys Thr Lys
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Lys Val Asn Thr Ala Asp Gln Cys Ala Asn Arg Cys Thr Arg Asn Lys
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Gly Leu Pro Phe Thr Cys Lys Ala Phe Val Phe Asp Lys Ala Arg Lys
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Gln Cys Leu Trp Phe Pro Phe Asn Ser Met Ser Ser Gly Val Lys Lys
485 490 495

Glu Phe Gly His Glu Phe Asp Leu Tyr Glu Asn Lys Asp Tyr Ile Arg
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Asn Cys Ile Ile Gly Lys Gly Arg Ser Tyr Lys Gly Thr Val Ser Ile
515 520 525

Thr Lys Ser Gly Ile Lys Cys Gln Pro Trp Ser Ser Met Ile Pro His
530 535 540

Glu His Ser Tyr Arg Gly Lys Asp Leu Gln Glu Asn Tyr Cys Arg Asn
545 550 555 560

Pro Arg Gly Glu Glu Gly Gly Pro Trp Cys Phe Thr Ser Asn Pro Glu
565 570 575

Val Arg Tyr Glu Val Cys Asp Ile Pro Gln Cys Ser Glu Val Glu Cys
580 585 590

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595 600 605

Ser Gly Lys Ile Cys Gln Arg Trp Asp His Gln Thr Pro His Arg His
610 615 620

Lys Phe Leu Pro Glu Arg Tyr Pro Asp Lys Gly Phe Asp Asp Asn Tyr
625 630 635 640

Cys Arg Asn Pro Asp Gly Gln Pro Arg Pro Trp Cys Tyr Thr Leu Asp
645 650 655

Pro His Thr Arg Trp Glu Tyr Cys Ala Ile Lys Thr Cys Ala Asp Asn
660 665 670

Thr Met Asn Asp Thr Asp Val Pro Leu Glu Thr Thr Glu Cys Ile Gln
675 680 685

Gly Gln Gly Glu Gly Tyr Arg Gly Thr Val Asn Thr Ile Trp Asn Gly
690 695 700

Ile Pro Cys Gln Arg Trp Asp Ser Gln Tyr Pro His Glu His Asp Met
705 710 715 720

Thr Pro Glu Asn Phe Lys Cys Lys Asp Leu Arg Glu Asn Tyr Cys Arg
725 730 735

Asn Pro Asp Gly Ser Glu Ser Pro Trp Cys Phe Thr Thr Asp Pro Asn
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Ile Arg Val Gly Tyr Cys Ser Gln Ile Pro Asn Cys Asp Met Ser His
755 760 765

Gly Gln Asp Cys Tyr Arg Gly Asn Gly Lys Asn Tyr Met Gly Asn Leu
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Ser Gln Thr Arg Ser Gly Leu Thr Cys Ser Met Trp Asp Lys Asn Met
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Glu Asp Leu His Arg His Ile Phe Trp Glu Pro Asp Ala Ser Lys Leu
805 810 815

Asn Glu Asn Tyr Cys Arg Asn Pro Asp Asp Asp Ala His Gly Pro Trp
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Cys Tyr Thr Gly Asn Pro Leu Ile Pro Trp Asp Tyr Cys Pro Ile Ser
Page 27

835

840

845

Arg Cys Glu Gly Asp Thr Thr Pro Thr Ile Val Asn Leu Asp His Pro
850 855 860

Val Ile Ser Cys Ala Lys Thr Lys Gln Leu Arg Val Val Asn Gly Ile
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Pro Thr Arg Thr Asn Ile Gly Trp Met Val Ser Leu Arg Tyr Arg Asn
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Lys His Ile Cys Gly Gly Ser Leu Ile Lys Glu Ser Trp Val Leu Thr
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Ala Arg Gln Cys Phe Pro Ser Arg Asp Leu Lys Asp Tyr Glu Ala Trp
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Val Leu Met Lys Leu Ala Arg Pro Ala Val Leu Asp Asp Phe Val Ser
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Thr Ile Asp Leu Pro Asn Tyr Gly Cys Thr Ile Pro Glu Lys Thr Ser
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995 1000 1005

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